

Topics in Primary Care Medicine

Immunizations for International Travelers

WENDY T. THANASSI, MD, *New Haven, Connecticut*

Each year more than 45 million Americans travel abroad for work or pleasure, and over 20 million of these travel to rural areas or developing countries. While the major medical risks of international travel are often exaggerated, the incidence of minor illness is not. Persons going to Asia, Africa, or Latin America for one month run a 65% to 75% chance of becoming ill, although only 1% will require hospitalization. The two most common illnesses that affect travelers, which do have immunizations and are often overlooked by physicians, are influenza and hepatitis A. The risk of illness to the traveler varies by health and age status, by the region to be visited, by the time of year, and by the length of the journey. Immunization advice for the traveler, therefore, is complicated and is best approached in a systematic manner. This article outlines six steps to sound immunization advice. These steps include ascertaining the traveler's special individual needs, routine immunization status, and routine travel immunization status, as well as the entry requirements for the country to be visited, geographically indicated vaccines, and immunizations as indicated for extended stays abroad.

(Thanassi WT. Immunizations for international travelers. *West J Med* 1998; 168:197-202)

The importance of appropriate immunization practices cannot be overstressed. In perhaps the greatest public health initiative the world has ever seen, broad administration of the vaccinia vaccine eradicated smallpox from the human population. With similarly high goals, the World Health Organization adopted a resolution to eradicate poliomyelitis by the year 2000. As of 1994, the Western Hemisphere was certified to be free of wild poliovirus and, to date, the number of poliomyelitis cases worldwide has been reduced by more than 80%.¹

A thorough pre-travel medical consultation, however, should include more than immunization advice. A review of malaria chemoprophylaxes, chemotherapies for traveler's diarrhea, food and water precautions, insect warnings, wilderness travel considerations (such as altitude and heat and cold issues), and even issues regarding safety from violence should be made a part of the traveler's particular itinerary. While these issues are beyond the scope of this article, several thorough references are available.^{2,3} (An excellent source of information is the website of the Center for Disease Control and Prevention [CDC] at www.cdc.gov.) Pre-travel preparation ideally begins 4 to 6 weeks before departure so that immunization schedules can be adequately spaced, vaccines can have time to take effect, and appropriate medications and supplies can be purchased.

All immunizations should be recorded on the yellow *International Certificate of Vaccination* card issued by

the World Health Organization. This card is commonly called "the yellow card," and it is given to the patient to keep. The cards are available from the Superintendent of Documents, US Government Printing Office, Washington DC 20402 (phone: 202/783-3238). The accompanying booklet has a page reserved for the official validation of yellow fever vaccination, which is required for entry into some countries.

The Approach

Determining the appropriate immunizations for international travelers is one of the most complex areas of travel medicine, and it poses great challenges to clinicians. A systematic and thorough approach to the immunization consultation will best ensure high-quality care for the traveler. Below is a proposed six-step approach⁴ to understanding and addressing the immunization needs of the traveler. The steps of the approach focus on determining:

- special needs of the traveler,
- routine childhood immunization status,
- routine travel immunization status,
- entry requirements of the country to be visited,
- geographically indicated vaccinations, and
- immunizations indicated for an extended stay abroad.

TABLE 1.—Preferred Childhood Immunization Schedule¹⁰

Vaccine	Age									
	Birth	1 Mo	2 Mos	4 Mos	6 Mos	12 Mos	15 Mos	18 Mos	4-6 Yrs	11-12 yrs
	////////// Hep B-1 //////////									
Hepatitis B		////////// Hep B-2 //////////			////////// Hep B-3 //////////					Hep B*
Diphtheria-tetanus-pertussis			DTaP	DTaP	DTaP		//////////DTaP//////////		DTaP	Td
Haemophilus influenzae type b			Hib	Hib	Hib	////////// Hib //////////				
Poliovirus			IPV	IPV		//////////OPV //////////			OPV	
Measles- mumps-rubella						////// MMR ////			MMR or	MMR
Varicella zoster						////////// Var //////////				Var*

* "catch-up" vaccinations

Determine the Special Needs of Travelers

The immunization needs of older people, pregnant women, children, and immunocompromised people (such as patients with cancer, HIV, or functional asplenia) may vary from the general recommendations. For healthy elders, a one-time pneumococcal vaccine and an annual influenza immunization should be administered. Older adults on gastric acid blockers should be considered for the cholera vaccine when traveling to endemic areas. Travelers with asplenia should receive encapsulated bacterial vaccines such as meningococcus and pneumococcus, and those with chronic obstructive pulmonary disease and asthma should have their pneumococcus and influenza immunizations updated. Other recommendations for travel by older people are consistent with those for the general population.

For the pregnant or immunocompromised traveler, live-virus vaccines (such as those for oral polio [OPV], measles-mumps-rubella [MMR], and yellow fever) and attenuated bacterial vaccines (such as oral typhoid) are contraindicated. A guide such as *Health Information for International Travel*, published annually by the CDC, is an excellent source for the most current advice on treating these special groups.

Immunization requirements for children travelers are similar to those for adults although the minimum age for each vaccine varies, and the doses are age-appropriate. It is important to note that the yellow fever vaccine is absolutely contraindicated in children younger than four months, and it is generally contraindicated in children younger than nine months.

Determine the Routine Childhood Immunization Status

The "routine" series of childhood immunizations should be current in all people but especially in travelers who may be exposed to the respective pathogens in their journey. The standardized routine childhood schedule is included in Table 1. Of note is the fact that

persons born overseas may have never received their primary immunization series.

Several important changes have recently been made to the routine childhood immunization schedule. In January 1997, the CDC's Advisory Committee for Immunization Practices changed their recommended use of the OPV in the primary series in children. Because vaccine-associated poliomyelitis has been the only indigenous form of the disease in the US since 1979, the new CDC recommendation is to use the enhanced injectable polio vaccine (eIPV) for the 2- and 4-month doses; the OPV is used for the last two doses in the childhood series, rather than for *all* doses (as was previously the practice). This is an interim revision and will be changed again in 3 to 5 years when a combination vaccine, which includes eIPV, should be available. Ultimately, when worldwide eradication of wild-type poliovirus is achieved, all poliovirus vaccination can be discontinued.⁵

Additionally, a new diphtheria-tetanus acellular pertussis vaccine (DTaP) was approved for use in June 1996. It has fewer side effects than the old formulation and is recommended as a replacement of the old diphtheria tetanus pertussis (DTP) vaccine for all four required doses. A new combination of Haemophilus influenza type B (Hib) and Hepatitis B vaccine (COMVAX) was licensed in October 1996, which will help to decrease

TABLE 2.—Preferred Adult Immunization Schedule *

Vaccine	Frequency	Dosage
Measles, Mumps and Rubella	Two doses at least 1 month apart.	0.5 ml IM
Poliovirus	Two doses at 4-8 week intervals, third dose 2-12 months after second.	0.5 ml SC
Tetanus and Diphtheria Toxoids combined	Two doses 4-6 weeks apart, third dose 6-12 months after second.	0.5 ml IM
Varicella	Two doses separated by 4-8 weeks.	0.5 ml SC

* adapted from the original. The information provided in Table 2 is for international travelers without contraindication to the vaccines and without previous immunizations.

the number of injections children receive. Finally, hepatitis B and the varicella zoster vaccines are included in the routine childhood schedule, and "catch-up" immunizations should be given to teens who missed their primary series.

Childhood Immunizations for Unimmunized Adult Travelers

Many adults, particularly those born overseas, have not completed their childhood series. These patients should be brought up-to-date on their tetanus-diphtheria (Td), MMR, and polio vaccines. For nonimmune travelers, varicella has been added to the list of indicated vaccines. The OPV is contraindicated in adults who did not receive a polio vaccine as a child. The immunization schedule for unimmunized adult international travelers is included in Table 2.

Boosters for Previously Immunized Adult Travelers

For adults who were last immunized as children, several boosters may be needed. Adults born after 1956 and before 1980 who have not had measles should receive an adult measles booster with either measles antigen alone or the MMR trivalent vaccine. Although the standard for nontraveler patients is a tetanus booster every 10 years, for the international traveler tetanus should be boosted if it has been more than five years since the last immunization. This recommendation protects the traveler against the disease and minimizes the chances of having to receive a postexposure injection in a potentially unsanitary hospital overseas. Several recent diphtheria outbreaks in Eastern Europe and the former Soviet States make the use of the combination tetanus-diphtheria (Td) vaccine the immunization of choice for travelers to this region.

A one-time adult polio booster is appropriate for travelers to developing countries in the Eastern Hemisphere. The OPV can be given to persons who were previously immunized against polio, are immunocompetent, and who are not in contact with immunocompromised people. This live virus can be shed in the stool, and fully 2 of every 3 cases of polio caused by the vaccine occur in immunocompromised people who were in contact with people who received OPV; the risk is 1 per 2.4 million doses. Both OPV and the newer eIPV show a 90% to 100% efficacy.

Determine the Routine Travel Immunization Status

Hepatitis A and typhoid fever are two of the three most common tropically-acquired febrile illnesses in returning travelers (malaria is the third). Influenza is both tropically and nontropically acquired and imparts great morbidity on travelers. Protection against these diseases should be provided for every traveler considered to be at-risk for acquiring these illnesses while abroad.

Hepatitis A

Hepatitis A is the most common vaccine-preventable disease in travelers, so assuring hepatitis A immunity is a

crucial part of any travel medicine consultation. Immunization should be considered for all travelers except those going to Western Europe, Australia or New Zealand, and Japan. Spread by contaminated food and water, the risk of hepatitis A to unprotected travelers ranges from 1 to 20 per 1000 people during a 4-week stay in a developing country. The risk is greatest for travelers to rural areas who stay in private homes.⁶ In the unimmunized traveler, hepatitis A infection is 10 to 100 times more common than typhoid fever (2 per 1000 to 10,000 people) and 1000 times more common than cholera infection (2 per 100,000).⁷ Despite this high incidence, one study of 400 US passengers at the departure gates of nonstop flights to high-risk destinations in Asia showed that 80% of the travelers were not immunized against hepatitis A.⁸

The new hepatitis A vaccines Havrix and Vaqta are changing the future of this disease for travelers. Although these immunizations take almost 14 days to reach peak efficacy, they are more than 90% effective and remain so for at least 10 years. Immune/gamma globulin takes only two days to reach full efficacy but is only 70% to 80% effective and lasts only 3 to 5 months (depending on the dose given). Therefore, for a one-time, short-stay traveler who plans to depart within two weeks, immune/gamma globulin is appropriate. For a traveler who intends to take multiple trips abroad or stay for more than five months, the hepatitis A vaccine is a better choice.

Typhoid Fever

Typhoid fever, caused by the enteric pathogen *Salmonella typhi*, is spread by fecally contaminated food and water. The incidence of typhoid fever among American travelers typically is low (58 to 174 per 1 million travelers), but 62% of all cases reported in the US are acquired abroad. Mexico, Peru, Pakistan, and India are the countries that present the highest transmission rates.

Immunizations against *Salmonella typhi* come in both oral and injectable forms and should be offered to those staying in endemic areas for over two weeks. The oral form has fewer side effects, but strict adherence to the every-other-day dosing should be emphasized; compliance with this regimen is apparently a considerable problem. The oral capsular vaccine, a live-bacterial preparation, is contraindicated in people who are immune-compromised or in household contact with immune-compromised persons. A liquid suspension vaccine is expected in the near future.

Influenza

Of febrile illnesses in travelers returning from trips abroad, 80% are due to commonly acquired diseases such as influenza. The influenza vaccine is often overlooked when making immunization recommendations, but it is perhaps the most relevant of all. The trivalent vaccine that is given in the US is equally effective around the world. Furthermore, influenza is present year round in tropical areas. (The influenza season south of the tropics is opposite that of the US, running from April

TABLE 3.—Countries Requiring Yellow Fever Immunization (as of December 1996)¹²

Africa	South America
Benin	French Guyana
Burkina Faso	
Cameroon	
Central African Republic	
Congo	
Cote d'Ivoire	
Gabon	
Ghana	
Liberia	
Mali	
Mauritania*	
Niger	
Rwanda	
Sao Tome/Principe*	
Senegal	
Togo	
Zaire	

* for a more than two-week stay

to November.) This inexpensive and effective vaccine should be offered to every person who will be traveling during an area's influenza season.

Determine the Entry Requirements of the Country to be Visited

Officially, yellow fever is the only vaccine required for entry into some countries, with the exception of Saudi Arabia during the Hajj. Certain African nations, however, sporadically "unofficially" request proof of cholera immunity upon entry. For travelers crossing multiple African borders that are "off the beaten track," one dose of the cholera vaccine meets the requirements for entry. This vaccine is politically mandated but not medically indicated.

Yellow Fever

The yellow fever vaccine is *required* by some countries as a condition for entry (Table 3). It is strongly *recommended* for all travelers to South America and rural areas of equatorial Africa, both of which are endemic regions containing infected *Aedes* mosquitoes that may spread the virus to travelers.

Yellow fever is so named for its predilection to cause jaundice. It can be as mild as a flu-like illness and as severe as hepatitis or hemorrhagic fever. This mosquito-borne disease rarely affects travelers; in the travelers who contract it, however, mortality rates may be as high as 50%. Fortunately, the vaccine has few side effects, only needs a booster every 10 years, and is nearly 100% protective.

The immunization is contraindicated in persons allergic to eggs, immune-compromised people, or those in contact with immune-compromised people. For travelers who meet these conditions, the "yellow card" has a section for "medically indicated exemptions."

Saudi Arabia—The Hajj

As of January 1998, Saudi Arabia is the only country that officially requires proof of meningococcal vaccinations for direct travel from the United States, and this requirement is in place only during the Hajj. The Hajj is a six-week annual pilgrimage to Mecca that takes place in the late spring. The exact dates of this event change every year. People traveling to Saudi Arabia should contact the consulate to determine the timing of the year's Hajj. The 1998 requirements are available from the World Health Organization (WHO) Weekly Epidemiological Record, No. 1/2, January 2–9, 1998.

Determine the Immunizations that are Geographically Indicated

Each area of the world has its own vaccine-preventable endemic pathogens. Knowing the itinerary of the traveler will help the consultant offer the appropriate protection.

Cholera

The current injectable cholera vaccine is only 50% effective, often causes gastrointestinal upset, and lasts for only 3 to 6 months. Due to these substantial limitations, the two-dose series is rarely recommended, except to people traveling to substantially high-risk areas such as central African refugee camps. It is also recommended for people taking H₂-blockers or those who have had a gastric resection—these people have a decreased resistance to the *Vibrio cholerae* bacteria. As discussed above, proof of cholera immunization is occasionally requested by African border guards.

Cholera is endemic in much of tropical Africa, Asia, and South America, but the limitations of the vaccine make its use questionable. An oral whole-cell cholera vaccine is already approved for use in Canada, and the US eagerly awaits its arrival.

Meningococcus

Meningococcal vaccine is another commonly indicated immunization for travelers. The current formulation protects against strains A, C, Y, and W-135. Because the most prevalent strains within the US are A and B, this vaccine is only minimally protective against *Neisseria meningitidis* in the US. Recent outbreaks of meningitis in Eastern countries make meningococcal vaccine prudent for travelers to Nepal, Northern India, and Saudi Arabia, as well as to the "meningitis belt" across sub-Saharan Africa.

Tick-Borne Encephalitis

Tick-borne viral encephalitis, also known as spring-summer encephalitis, occurs in forested areas of

Europe (including Scandinavia) and the former Soviet states. The risk for contracting the disease is greatest for persons traveling, camping, or hiking in woods, fields, or pastures between April and August—the time in which *Ixodes ricinus*, the principal carrier tick, is most active. Drinking unpasteurized dairy products may also result in infection. The immunization currently is not available in the United States but can be obtained in Europe for travelers considered at-risk for contracting the disease.

Yellow Fever

Even when not required for entry, this immunization should be given to travelers who are staying more than one week in a yellow fever endemic area, such as equatorial South America or Africa. Yellow fever does not exist in Asia.

Provide Extra Immunizations for Extended Stays

Clearly, the longer a person travels, the greater the risk of contracting an endemic disease. In addition to following all of the information and guidelines provided above, if the traveler is staying for more than one month overseas, the hepatitis B, Japanese encephalitis, and rabies immunizations should be considered.

Hepatitis B

Ideally, everyone should be immunized against the hepatitis B virus. In the past, immunization was recommended only for travelers staying abroad for over six months. There are between 250,000 and 300,000 new infections caused by hepatitis B every year in the US, however, so the recommendations for immunization have become much more strict. The CDC now suggests that all sexually active adults with more than one partner in the past six months should be encouraged by their physicians to receive the three-dose vaccine series, regardless of their sexual plans while abroad. Most infections are clearly sexually transmitted, but transmission also may occur from parenteral exposure to this virus.

Japanese Encephalitis

Epidemics of Japanese encephalitis have dotted the Far East in recent years. A viral disease spread by chiefly by *Culex vishnui* mosquitoes, Japanese encephalitis is extremely rare, but it imparts grave morbidity on its recipient. The estimated risk is 1 per 5000 per one month stay or 1 per 20,000 per one week stay in endemic areas during the transmission season. Transmission is highest after the rainy season, when mosquitoes are prevalent. In China and Korea, this is in the summer and fall; in India, Nepal, and Sri Lanka, the season is October to December. In tropical areas, sporadic cases can occur any time of the year. Urban areas on tourist routes are not considered to be high-risk areas; however, travelers frequenting such rural environments as pig farms or rice paddies in Southeast Asia should

consider vaccinating against Japanese encephalitis. Of importance is the fact that minor local reactions, such as redness, swelling, and pain, occur in 10% of recipients. Serious allergic effects, including hives and angioedema, are reported in 0.1% of those who received the vaccine. The side effects can occur after any of the three doses and can be delayed for up to two weeks. Travelers receiving the vaccine should remain in the doctor's office for 30 minutes following immunization, to watch for immediate hypersensitivity reactions.

Rabies

A less common disease, rabies, also must be considered by people traveling for extended periods of time. Rabies is a rare but invariably fatal infection of the brain transmitted by contact with the saliva of an infected animal. Dogs are the world's major reservoir of rabies. In Thailand, an estimated 8% of all street dogs are infected with rabies. A recent study of travelers to Thailand found that 1.3% had been bitten and 8.9% had been licked by a dog during their stay.⁹ Despite these statistics, only five cases of imported rabies occurred in Americans over a 12-year period, from 1980 to 1992.⁷ On October 20, 1997, the Food and Drug Administration licensed a new rabies vaccine (RabAvert), which allows greater flexibility in treatment choices for people who are sensitive to other vaccines.

Plague

People with *Yersinia pestis* infection, commonly known as the plague, experience the rapid onset of fever, chills, headache, myalgias and malaise. The pneumonic form is further characterized by cough and shortness of breath and the bubonic form by painful swelling of the lymph glands (buboes) in the neck, axilla, or groin. Untreated, the plague is fatal in more than 50% of cases. Plague is carried by fleas, rodents, cats, and humans, and it is transferred to people through flea bites or the inhalation of airborne pneumonic plague droplets. The risk of contracting plague, even in endemic areas, is extremely small. The efficacy of the plague vaccine has not been demonstrated in a controlled trial in humans. Immunization should only be considered for field researchers or those who anticipate intense exposure to rodents in the rural mountainous regions of Africa, Asia (including India), and the Americas. Vietnam is currently the country of greatest concern.

Summary

The six steps outlined in this article to providing sound immunizations for international travelers are general guidelines only; individual needs may vary. Nonetheless, it is important that health care professionals work from a framework such as the one presented here to ensure that the immunization consultation is both appropriate and thorough.

REFERENCES

1. Centers for Disease Control. Progress toward global eradication of poliomyelitis, 1985–1994. MMWR 1995; 44:273–275;281

2. Reyes I, Shoff W. General medical advice for travelers. *Emerg Med Clin North Am* 1997; 15:1–17
3. Thanassi WT, Weiss EL. Preparing patients for tropical travel. *Hosp Med* 1997; 33:47–58
4. Thanassi WT, Weiss EL. Immunizations and travel. *Emerg Med Clin North Am* 1997; 15:43–89
5. Centers for Disease Control. Poliomyelitis prevention in the United States: introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine. *MMWR* 1997; 46:1–3
6. Steffen R. Risk of Hepatitis A in travelers. *Vaccine* 1992; 10:S69–S72
7. Kozarsky P. Maximum immunization for travel. *J Travel Med* 1995; 2:186–191
8. Abhyankar SA, Thanassi WT, Gianotti AJ, Weiss EL. US Travelers Neglecting to Seek Pre-Travel Medical Care. Presentation at the International Society of Travel Medicine: Geneva, Switzerland, March 1997
9. Dawood R. Maximum immunization for travel. *J Travel Med* 1995; 2:186–187
10. Centers for Disease Control and Prevention. Childhood Vaccination Schedule, United States, January–December 1998. January 16, 1998
11. Centers for Disease Control and Prevention. Adult Immunization Schedule, January–December 1997. January 24, 1997; Available from www.cdc.gov/nip/adult.htm
12. Division of Quarantine, National Centers for Infectious Diseases, Centers for Disease Control and Prevention. Comprehensive Yellow Fever Vaccination Requirements; October 18, 1996. Available from www.cdc.gov/travel/yelfever.htm#instructions